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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1648	10

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/989,620	SERIZAWA ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,5,6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of the species of the claimed invention wherein the compound having a folate antagonistic or a dihydrofolate reductase inhibiting activity is methotrexate in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the examiner did not make the species requirement as a Markush type claim. This is not found persuasive. There are two basic requirements for the application of the Markush practice as describe din MPEP § 803.02. These requirements are 1) that the members of the Markush group share a common utility, and 2) that the members share a substantial structural feature disclosed as essential to that utility. Markush practice is only applied where the claimed inventions satisfy these requirements.

The presently claimed invention does not meet both of these requirements. The examiner agrees that the members of the claimed group of inventions share a common utility in the method of the present claims. However, the application nowhere identified any structural feature that is essential to that function. Rather, the claims and description merely require that the compounds have a particular function and effect. While the applicant does list a number of structures in the application, no common feature essential to these functions are identified, and no correlation between the structures and the desired synergistic effect of the compounds is made. Therefore, while the applicant has satisfied the first requirement for the application of Markush practice, the applicant has not satisfied the second.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

1. The information disclosure statement (IDS) submitted on January 29, 2002, and entered as paper number 5, is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

2. The following references are in a foreign language accompanied by an English abstract. Due to this, the references have been examined only to the extent of the disclosure in the abstract.

Nakayama et al., Mebio, 12(10): 79-86.

Aono et al, 38th Japan Rheumatic Society Summary Collection, (1994), p. 487.

Serizawa, Saishin-igaku 54(4):917-924.

Fujisawa, Molecular Medicine 33:1254-1261.

3. The reference JP 5-503281 in the IDS of paper 5 is in a foreign language and has none of a translation, an explanation of its relevance, or an English abstract. The reference has therefore been placed in the file, but has not been considered.

4. It is noted that for the McCarty reference "Arthritis and Allied Conditions," the applicant supplied only a copy of the table of contents. As such, the reference has been considered only to the extent of the information contained in the table.

5. It is noted that the IDS filed on January 29, 2002, and entered as paper number 6, is a duplicate of paper number 5. The IDS has therefore been entered in to the case, but has not been independently considered as the references cited therein have been considered in the IDS of paper number 5.

6. The supplemental IDS entered as paper number 4 was filed so as to submit a reference cited in, but not provided with, the IDS of paper number 5. The reference will be considered in paper number 5.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-8, 14-22, 27, 30-37, and 42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1 and 14 will be treated as representative of the rejected claims. Claim 1 reads on a pharmaceutical composition comprising (a) an anti-human Fas antibody with an apoptosis inducing activity and (b) a compound having a folate antagonistic or a dihydrofolate reductase inhibiting activity wherein the relative amounts

of (a) and (b) are such that they exhibit a synergistic apoptosis inducing activity. Claim 14 describes a method of using such a composition for the prevention of treatment of a disease treatable of preventable by an agent having apoptosis inducing activity.

These claims are rejected for two reasons. First, the applicant has not provided any guidance towards any compounds other than those listed, for example, in claim 5 that may have a synergistic effect when combined with the apoptosis-inducing antibody. Second, the applicant has not shown that any of the identified compounds other than methotrexate has such an effect. The claims read on a product, and method of using it, taking advantage of the claimed synergistic effect. The applicant explains in the application that synergism is a "coordinated or correlated action that is far stronger than would be expected by a person of ordinary skill in the art.' Thus, according to the applicant, this synergy is inherently unpredictable.

However, while the applicant has shown that such synergy exists between an anti-human Fas antibody and methotrexate (pages 28-29), the applicant has not established this synergy for any other of the claimed compounds, or provided any guidance in the application that would lead those in the art to other compounds having such synergy. While the applicant does require that these synergistic compounds (to the antibody) have one of two activities, the applicant has not established that these activities are, in themselves, determinative of the presence of the synergy. Thus, the claims read on a broad class of compositions based on a specification disclosing only a single working example.

A brief discussion of the 35 U.S.C. 112 ¶ 1 written description support requirements for broad classes of inventions (a genus) is provided in section 2163 of the Manual of Patent Examination Procedure. The MPEP states:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed. In the present case, only a single example has been shown. Further, the applicant has provided no correlation between the characteristics of the claimed species of the invention, other than methotrexate, and the activity required in the claim language (the synergism). Absent such a correlation, or other evidence that members of the described genus all share the claimed activity, the applicant has not provided an adequate written description such that one skilled in the art would know that the applicant was in possession of the full scope of the claimed invention.

9. Claims 1-8, 14-22, 27, 30-37, and 42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions, and methods of treating rheumatoid arthritis using the composition, comprising an anti-human Fas antibody and methotrexate, does not reasonably provide enablement for compositions or methods wherein the composition comprises the claimed antibody and any "compound having a folate antagonistic or dihydrofolate reductase inhibiting activity." The specification does not enable any person skilled

in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The claims have been described above. As indicated above, the applicant has not shown that the claimed synergistic effect is present in the combination of the claimed antibody any of the other claimed compounds other than methotrexate.

In the application, synergism is indicated to be a "coordinated or correlated action that is far stronger than would be expected by a person of ordinary skill in the art." Page 3. Thus, according to the applicant's definition (and the definition recognized in the art generally), such synergism is inherently unpredictable. Where there is unpredictability in the art, a more detailed disclosure is required than would be necessary for more predicable subject matter. See generally, MPEP § 2164.03. In the present case, the applicant has provided only one working example of a combination of compounds resulting in such synergism; that of a CH11 antibody and methotrexate. No other guidance as to what other compounds would have the desired results has been provided.

It is noted that the applicant has both identified compounds "having a folate antagonistic or dihydrofolate reductase inhibiting activity" generally, and some specifically, in the description and the claims. However, the application nowhere draws any correlation between these activities and the synergistic effect. I.e., the applicant has neither provided any evidence that these activities led to the synergistic effect of methotrexate, nor shown that any other compounds with this activity had the synergistic effect. Thus, the claims appear to be setting two distinct and unrelated limitations on the non-antibody compound. First, it must have one of the two stated functions, and secondly, it must achieve synergism with the anti-Fas antibody. While one skilled

in the art may know which compounds fulfill the first limitation, absent further teachings by the applicant, one of ordinary skill in the art would not know, or have any guidance towards, other compounds within that group that also satisfy the second limitation.

10. Claims 1-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of making and using a synergistic composition of methotrexate and the two identified antibodies, does not reasonably provide enablement for such compositions with any anti-Fas antibody. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. These claims read on compositions and methods comprising a composition of anti-Fas monoclonal antibodies, and methotrexate. The antibodies are further identified in the claims as CH11 or HEF7A antibodies, or humanized antibodies thereof.

Although the applicant's claims read on compositions of any anti-Fas antibodies, or humanized forms of the CH11 and HEF7A antibodies, the applicant is not enabled for such. The specification of the application teaches that the combination of the identified antibodies and methotrexate lead to a synergistic effect on the therapeutic value of the antibodies. However, the art also teaches that this synergistic effect is not present in many anti-Fas antibodies. See e.g., McGahon et al, British Journal of Haematology 101:539-547; and Mizutani et al, American Cancer Society, 79(6): 1180-89 (both of record in the IDS filed as paper 5). These references each teach that methotrexate does not yield synergistic apoptotic effects in cells with any anti-Fas antibody, although McGahon does teach that the compound yields synergy with some such

antibodies (IgM). Mizutani, page 1183; and McGahon, pp. 542 and 546 (text paragraph spanning these two pages). As the art teaches that methotrexate sometimes, but does not always yield synergistic effects when combined with anti-Fas antibodies, the applicant is not enabled for claims requiring such synergy between methotrexate and any such antibody.

11. Claims 14-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims read on methods of preventing or treating a disease comprising administering to a mammal the claimed composition. The diseases for which the claims may be used are described as "preventable or treatable by an agent having apoptosis inducing activity." The claims are rejected because the applicant has not described, or provided guidance leading to, all such diseases.

The applicant has identified rheumatoid arthritis, and a number of autoimmune diseases (and autoimmune diseases generally) as being so treatable. However, the remaining diseases are being identified by a desired characteristic (that they be treatable by the claimed composition). This is comparable to claims to products by their desired function. With regards to such, the Federal Circuit court has stated that a product that has been defined by function or result alone does not meet the written description requirement. Enzo Biochem Inc. v. Gene-Probe Inc., 63 U.S.P.Q.2d 1609, at 1612-13. The court continued to state that a functional characteristic may provide descriptive support "when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. Thus, in the present

case, the applicant would have to supply some other characteristic of the claimed diseases that correlates with it susceptibility to treatment by the claimed composition, in order to satisfy the description requirement. No such correlation is present in the application at issue.

The applicant has identified autoimmune diseases and rheumatoid arthritis as potential diseases for which the claimed method may be used. However, the applicant has not identified what about these diseases makes them so susceptible, such that one skilled in the art would recognize other diseases than those specifically mentioned for which the method could be used. Absent such a correlation, the applicant has not provided a sufficient description to support the claimed method to the extent that the read on methods of treating any disease susceptible to treatment by the claimed composition.

12. Claims 1-3, 6-7, 9-11, 13-17, 19-21, 23-25, 27-32, 34-36, 38-40, 42, and 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods compositions, and methods of treating rheumatoid arthritis using compositions, of methotrexate and an anti-Fas antibody, does not reasonably provide enablement for the compositions and methods wherein the antibody is CHII. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. For the purposes of this rejection is assumed that CH11 represents a specific monoclonal antibody to the Fas protein. However, the application nowhere provides any indications as to how to recognize, or make this antibody, or from where it may be acquired. Absent such information, the applicant is not enabled for claims to compositions and methods comprising this antibody.

13. Claims 14-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating rheumatoid arthritis by administering to a human a composition comprising an anti-human Fas antibody and an compound have a folate antagonistic or a dihydrofolate reductase inhibiting activity, does not reasonably provide enablement for methods of treating or preventing any autoimmune disease or rheumatoid arthritis in any mammal using the claimed compositions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. For the purposes of this rejection, the claims are being interpreted as describing method of preventing or treating, an autoimmune disease or rheumatoid arthritis, in any mammal (including humans), by administering to the mammal a composition comprising an anti-human Fas antibody and a second compound as described above.

These claims are being rejected for three reasons. First, the applicant has not enabled the claimed method to the extent that it reads on method of preventing the identified diseases. Second, the applicant has not shown that the claimed method would be effective in treating any autoimmune disease. Third, the applicant has not shown that a composition comprising an anti-human Fas antibody would be effective in inducing apoptosis in any mammal.

The application has not shown that the claimed composition is effective for the prevention of the identified diseases.

In the application, the applicant has demonstrated that the claimed composition is effective for inducing apoptosis in a human cell line in vitro. However, the applicant has not

shown that the administration of the claimed composition would be effective for the prevention of the identified diseases. More particularly, the applicant has not shown that the claimed method would be effective in preventing any autoimmune disease. While treatments and preventatives for rheumatoid arthritis are known, there are many autoimmune diseases for which no preventative is known. This is the case even though the constituents of the currently claimed composition were known and used in the art for the treatment of some forms of autoimmune diseases. In view of this, absent some evidence that the claimed composition does prevent these diseases, the applicant is not enabled for such.

However, the only evidence of the efficacy of the claimed composition provided by the applicant does not demonstrate prevention. In the example provided on pages 28-29 of the application, the applicant showed that the claimed composition resulted in a "significant increase" in the apoptosis inducing activity as compared to the anti-Fas antibody alone. The tests are run against cells in vitro that are already exhibiting a disorder subject to the claimed treatment. There is no demonstration that no such disorder was prevented in normal cells after treatment with the claimed composition.

Further, the target cells of the experimental treatment were not disclosed as being completely killed in the experimental in vitro environment. Given that the uncontrolled environment within a living being is likely to inhibit the activity of a given drug in vitro, and the fact that unhealthy cell survived the treatment in vitro, it is unlikely that the claimed method would be effective in killing off all of the diseased cells in vivo. Thus, it is also unlikely that the composition would be able to kill off all such cells to the point where the disease does not arise in the first place. Therefore, although the claimed method may reduce the effects of some of the

identified diseases, the applicant has not demonstrated that the method would be effective in preventing these diseases.

The application does not enable the claimed method in the treatment of any autoimmune disease.

The claimed invention reads on methods of treating diseases by inducing apoptosis of cells in mammals. Among the diseases identified as subject to treatment by the claimed method are autoimmune diseases. However, the applicant has not shown that the claimed method would be effective in treating any autoimmune disease. Although the claims specify that such diseases must be "preventable or treatable by an agent having apoptosis inducing activity," because the applicant has not provided any means by which such a disease may be recognized other than by attempting to treat it, the limitation is not found enabled (see above), and therefore is not being considered in this rejection. The applicant teaches on page 32 of the application that the claimed composition is useful as an excellent agent for the treatment of autoimmune diseases.

The prior art also discloses that links between certain autoimmune diseases and "abnormalities in the Fas/Fas ligand system" and Fas related apoptosis were known. See e.g. Serizawa, EP 0909806, pages 2-4; and Holoshitz, U.S. Patent 6,098,631, columns 1-2. Both of these references taught that the induction of apoptosis was known to be an effective way of treating rheumatoid arthritis. Serizawa, page 3, lines 25-30; Holoshitz, claims. However, the Serizawa reference also indicates that Fas induced apoptosis is a cause, and not a cure for several autoimmune diseases. Page 3, paragraphs 0017-0018, page 0024. See also, Chittenden et al., U.S. Patent 6,221,615, column 3, line 57 to column 4, line 2 (teaching that autoimmune diseases

may be disorders characterized by inappropriate cell death, and therefore treated with an apoptosis inhibitor). Thus, while the art indicates that inducing apoptosis is an effective treatment for treating some autoimmune diseases, the treatment is not universally applicable. Rather, the art teaches that cellular apoptosis is a cause, or a least a symptom, of other forms of autoimmune disease. Therefore, the method claimed by the applicant would not be effective for the treatment of any autoimmune disease.

It is noted that the presence of non-operative embodiments in a claimed invention does not necessarily mean that the applicant is not enabled for that claim. However, "claims reading on significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative." MPEP § 2164.08 (b) (citing Atlas Powder Co. v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984); and In re Cook, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971)). In the present case, the applicant has not provided any means by which one skilled in the art would know whether or not the claimed method would be effective in the treatment of a particular disease. For any given disease, such a person would be required to identify the cause of the disease, and determine whether or not the induction, or the inhibition, of apoptosis would be the more appropriate response. Because the applicant does not teach any characteristic by which one skilled in the art could tell if a particular autoimmune disease required the claimed treatment, the applicant is not enabled for the claimed method as it extends to any autoimmune disease.

The applicant is not enabled for a method comprising administering a composition of anti-human Fas antibody to treat a disease in any mammal.

The last basis for the enablement rejection of these claims is that the applicant has not shown that an antibody specific for the human Fas protein receptor would be effective in inducing apoptosis in any mammal. The claims have been limited to compositions comprising anti-human Fas antibody. However, the claims also allow for the treatment of diseases in any mammal. Antibodies are generally specific to particular protein sequences. Thus, an antibody that is specific to a protein from one source may not recognize a homologous protein from another source. In the present case, the claimed composition contains an antibody specific to a human protein. Further, the only working examples provided by the applicant demonstrate that an anti-human Fas antibody can induce apoptosis in a human cell line. The applicant has not shown that these antibodies would be effective in inducing apoptosis in other mammals.

The applicant has not provided any teachings or evidence that an antibody targeting the human Fas protein would be effective in binding to, and inducing apoptosis in, cells exhibiting Fas proteins other that human Fas. Nor has the applicant demonstrated that the binding site necessary for apoptosis induction is homologous among these Fas proteins of different mammalian species. The applicant is therefore not enabled for a method of treating a disease in any mammal by administering an apoptosis inducing antibody specific to the human Fas protein.

14. Claims 2-4, 6-8, 10-13, 16-18, 20-22, 24-26, 28, 29, 31-33, 35-37, 39-41, and 43 are rejected for lack of enablement. The antibodies CH11 and HFE7A are required to practice the claimed invention described by these claims. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of cell lines

producing these antibodies. See 37 CFR 1.802.Because one cannot practice the claimed invention without the antibodies, access to them is required to enable the invention. The specification does not provide a repeatable method for readily identifying these antibodies without access to the cell lines producing them. The applicant has not provided any description of the antibodies other than their cell line references, and, for the HFE7A, an accession number without the required statements by the applicant.

Deposit of the cell lines producing these antibodies in a recognized deposit facility would satisfy the enablement requirements of 35 U.S.C. 112, because the strains would be readily available to the public to practice the invention claimed, see 37 CFR 1.801- 37 CFR 1.809.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination, or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1, 5, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Mizutani et al., American Cancer Society, 79(6): 1180-89. The claims read on a composition comprising an anti-Fas antibody and methotrexate. Such a composition is described by the reference. See e.g. page 1183. Although the reference does not teach a claimed characteristic of the claimed compositions, the reference does anticipate the claimed structure. The applicant cannot distinguish from the prior art based on the function of the claimed composition. See, MPEP § 2114. Thus, the reference anticipates the claims.

17. Claims 1, 5, and 9 are rejected under 35 U.S.C. 102(a) as being anticipated by Mizutani et al., J. Urology 160:561-570. The claims read on a composition comprising an anti-Fas antibody and methotrexate. Such a composition is described by the reference. See e.g. page 568. Although the reference does not teach a claimed characteristic of the claimed compositions, the reference does anticipate the claimed structure. The applicant cannot distinguish from the prior art based on the function of the claimed composition. See, MPEP § 2114. Thus, the reference anticipates the claims.

18. Claims 1, 5, and 9 are rejected under 35 U.S.C. 102(a) as being anticipated by McGahon et al, British Journal of Haematology 101:539-47. The claims have been described above. The

reference teaches a composition of anti-Fas antibody and methotrexate wherein the combination lead to a synergy of the apoptotic effects of the compounds. Pages 542 and 546, and Figure 7.

Conclusion

19. No claims are allowed.

20. The following prior art references are made of record and are considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

Whittaker, U.S. Patent 5,952,499 or Barnett et al, U.S. Patent 5,633,373, or Gross, U.S. Patent 6,153,615. Each of the references of Whittaker, Gross, and Barnett teach that such compounds are useful therapeutics for the treatment of rheumatoid arthritis. Whittaker, column 12, lines 17-29; Barnett, column 1, lines 34-45, and Gross, column 4, lines 43-57. Further, the compound identified in each of these references is methotrexate.

EP 0897724 A1. This reference, made of record in the IDS of paper 5, is considered to be redundant to the teachings of Gross, Whittaker, and Barnett applied above.

WO 91/10666. This reference teaches other dihydrofolate reductase inhibitors that are described as usable to treat rheumatoid arthritis. Page 2. Thus, this reference is considered applicable to claims 1-4 as redundant to Gross, Whittaker, and Barnett.

EP 0909816 and EP 0709097 (of record in the IDS filed as paper 5). These references teach the two identified anti-Fas antibodies and identify them as useful in the treatment of rheumatoid arthritis.

21. Note regarding the EP 0909816 and EP 0709097 references. It is noted that these references disclose the antibodies according to the claimed composition. Normally these references would be used to reject the claimed composition under 35 U.S.C. 103(a), in this case as obvious over the references cited under 102(a) or (b) above. However, these claims read on compositions with an unexpected characteristic: a synergistic reaction between the antibodies and methotrexate. This synergy is taught by the art references as being found only with IgM antibodies, and not with any anti-Fas antibody. The disclosed CH11 and HFE7A antibodies are not disclosed as IgM. Thus, one of ordinary skill in the art would not have expected the claimed synergy to be present, rendering claims to compositions of these antibodies and methotrexate apparently non-obvious. The references are therefore not applied as art in an obviousness rejection.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
March 19, 2003

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